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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,677	09/14/2001	Christine Libon	PF95PCTSEQ/D	9128
25666	7590	09/08/2004	EXAMINER	
THE FIRM OF HUESCHEN AND SAGE 500 COLUMBIA PLAZA 350 EAST MICHIGAN AVENUE KALAMAZOO, MI 49007			NAVARRO, ALBERT MARK	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/936,677

Applicant(s)

LIBON ET AL.

Examiner

Mark Navarro

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 29-58 and 60-64 is/are pending in the application.
- 4a) Of the above claim(s) 29-44, 52-55, 60 and 61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 45-51, 56-58 and 62-64 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

### **DETAILED ACTION**

Applicants amendment filed March 23, 2004 has been received and entered. New claims 62-64 have been added. Consequently claims 29-58 and 60-64 are pending in the instant application, of which claims 29-44, 52-55, and 60-61 have been withdrawn from further consideration as being drawn to a non-elected invention.

Applicants attention is drawn to the most recently filed claims which are non-compliant. Each claim must be identified with an appropriate status identifier, currently amended, canceled, etc. Applicants current claim set starts with claim number 29. Appropriate correction is required.

All grounds of rejection in the Office Action mailed December 23, 2003 are withdrawn.

The following new grounds of rejection are applied to the claims:

#### ***Claim Rejections - 35 USC § 112***

1. Claims 50-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of stimulating an immune response, does not reasonably provide enablement for methods of preventing cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed towards methods of preventing cancer.

Facts that should be considered in determining whether a specification is enabling, or if it would require an undue amount of experimentation to practice the invention include: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1403 (Fed. Cir. 1988). The Federal Circuit has noted, however, that only those factors that are relevant based on the facts need to be addressed. See Enzo Biochem. Inc. v. Calgene, Inc. 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir. 1999).

Cheng et al (IEEE transactions on medical imaging, Vol. 17, No. 3, June 1998, pp 442-450) set forth that the etiology of breast cancer remains unknown, so that “primary prevention becomes impossible.” (See abstract).

Burton (CA Cancer J. Clin Vol. 50, No. 4, pp 209-213, 2000) set forth that although there is good evidence that human melanoma is immunogenic and that the immune system can respond, vaccines have, as yet, no established place in the management of the disease.

A vaccine/prevention “must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough.” In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Given the lack of guidance, lack of working examples, and unpredictable nature of the invention as shown by Cheng et al and Burton et al, one of skill in the art would be forced into excessive experimentation to practice the broadly claimed invention.

2. Claims 45-51, 56-58, and 62-64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite in the recitation of “in need thereof.” One of skill in the art would be unable to determine the metes and bounds of the claimed invention. For instance, what conditions would be used to determine if the individual was in need thereof? Similarly, what conditions would be used to exclude an individual as not being in need thereof? Without a clear definition as to the metes and bounds of the term “in need thereof” one of skill in the art would be unable to determine the metes and bounds of the claimed invention.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 56-58, and 63-64 are rejected under 35 U.S.C. 102(b) as being anticipated by d'Hinterland et al.

The claims are directed to a pharmaceutical composition comprising a membrane fraction of Gram-negative bacteria, comprising proteoglycans, for administration in combination with an anticancer treatment in an amount effective to

stimulate an immune response and/or induce an antitumor immune response in a mammal, including a human, in need thereof.

d'Hinterland et al (US Patent Number 4,501,693) disclose of isolated membranous proteoglycan from *K. pneumoniae* which activates sharply the stimulation of NK cells. (See column 1).

It is noted that the claims recite "for administration in combination with an anticancer treatment." However, this is merely an intended use of the claimed composition, and as such is not afforded any patentable weight.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 45-49, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over d'Hinterland et al in view of Henderson and Teicher et al.

The claims are drawn to a method of stimulating an immune response and/or inducing an antitumor immune response in a mammal, including a human, in need thereof whereby a membrane fraction of Gram negative bacteria, comprising proteoglycans is administered in the form of a pharmaceutical composition in combination with an anticancer treatment in an amount effective to result in such induction and or stimulation.

The teachings of d'Hinterland et al are set forth above.

d'Hinterland et al do not teach of anticancer treatments.

Henderson (US Patent Number 5,648,478) teach of tumor vaccines which elicit NK cells to destroy tumor cells. (See column 14).

Teicher et al (US Patent Number 5,776,898) teach of standard treatments for tumors, including antiangiogenic agents, and chemotherapy. (See column 7).

Given that 1) d'Hinterland has taught that membranous proteoglycan isolated from *K. pneumoniae* stimulates NK cells, and that 2) Henderson et al has taught of tumor vaccines which elicit NK cells to destroy tumor cells, and that 3) Teicher et al have taught of standard modalities for treating cancer, including antiangiogenic agents and chemotherapy, it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have incorporated the composition of membranous proteoglycan isolated from *K. pneumoniae* as taught by d'Hinterland et al and combined

the composition with the tumor vaccine taught by Henderson. It would have been further obvious to combine standard cancer treatment such as chemotherapy as taught by Teicher since they both result in the same end effect, a destruction or slowing the growth of a tumor. One would have been motivated to combine the tumor vaccine and the proteoglycans isolated from *K. pneumoniae* in view of the shared mechanism of action, the stimulation of NK cells.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Navarro whose telephone number is (571) 272-0861. The examiner can normally be reached on 5/4/9.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Mark Navarro  
Primary Examiner  
September 2, 2004